

REMARKS

Applicants contend that the amendments are fully supported by the application as filed, and that no new matter has been or was intended to be added to the claims by virtue of these amendments, and the amendments are intended to be clarifying in nature. For ease of reference, note that Claims 4, 7-9, 11, 13-15, 35-36, 40, 59-60, 72, 74-76, 80-81, 83-89, and 96 are presently cancelled, and claims 41-42, 71, 73, 77, 82, and 90-94 remain pending. Entry of the amendments and favorable consideration of the claims is requested.

Claim Objections

The Office has objected to the absence of Claims 61-70. Applicants have corrected the listing of claims accordingly and thank the Examiner for the careful review of Applicants' claims.

Rejections under 35 USC §112

The Office has rejected claims 4, 7-9, 11, 13-15, 35-36, 40-42, 59-60, 71-94, and 96 as rejected indefinite under 35 USC §112, first paragraph, asserting that the term "rapidly and completely dissolve on moist surfaces" is a relative term which renders the claim indefinite.

Applicants first note that Claims 4, 78-79, and 85 were previously cancelled, and the rejection to these claims is therefore inapplicable. With respect to the claims now pending, Applicants note that the rejected language was amended in Applicants prior response such that the rejected phrase is no longer recited in the claims.

To the extent the Office intended to object to the phrase "rapid dissolving tablet suitable for buccal delivery" as recited in independent claim 71, Applicants respectfully contend that the art makes clear that one of ordinary skill in the art would reasonably conclude that Applicants' disclosure adequately described the claimed invention at the time of filing. When a disclosure describes a claimed invention in a manner that permits one skilled in the art to reasonably conclude that the inventor possessed the claimed invention the written description requirement is satisfied. (MPEP §2163). This possession may be shown in any number of ways and an Applicant need not describe every claim feature exactly because there is no *in haec verba*

requirement. (MPEP § 2163). Rather, to satisfy the written description requirement, all that is required is “reasonable clarity.” (MPEP § 2163.02). An adequate description may also be made in any way through express, implicit, or even inherent disclosures in the application, including words, structures, figures, diagrams, and/or formulae. (MPEP §§ 2163(I), 2163.02).

Applicants contend that the phrase “rapid dissolving tablet suitable for buccal delivery” is readily understood by one of ordinary skill in the art such that the metes and bounds of the claim scope would be readily apparent. Applicants contend that as such, the requirements of 35 USC §112, first paragraph, are met. Applicants continue to refer the Office to the Declaration of Mike Triplett, of record, in support. Applicants further submit the article “Drug-delivery Products and the Zydis Fast-dissolving Dosage Form,” Seager, J. Pharm. Pharmacol. 1998, 50; 375-382, received September 1997 and published 1998, submitted herewith, further demonstrates that a fast-dissolving (or rapid-dissolving) formulation was, at the time of filing, a type of formulation that was readily understood by one of ordinary skill in the art. For example, in Seager, it is stated that

... [o]ne new drug-delivery technology that has been developed to the production scale of operation in recent years, and which is being used to develop and commercialize an increasing number of products, is that of the Zydis fast-dissolving dosage form....

Seager, at p. 376.

Seager further describes this dosage form as “not requir[ing] water to aid swallowing” and states that “[w]hen Zydis units are put into the mouth the freeze-dried structure disintegrates instantaneously releasing the drug which dissolves or disperses in the saliva.” Applicants contend that the absence of a specific recitation of disintegration time in this reference is evidence that a rapidly dissolving tablet suitable for buccal delivery is readily understood in relevant the art. As such, Applicants respectfully contend that the term “rapid dissolving tablet suitable for buccal delivery” is a term known in the art such that the term adequately meets the requirements of 35 USC §112, second paragraph. Withdrawal of the rejection on this basis and reconsideration of the claims is respectfully requested.

Rejections under 35 USC §103

Claims 7-9, 11, 13-15, 35-36, 40-42, 59-60, 71-77, 80-84, and 86-94 were rejected under 35 USC §103 over Coffee (WO 98/03267) in view of Barabas (US 4,704,436), Liu et al (US 6,465,009) and Murray et al (US 6,709,669).

Under MPEP §2142, the Office bears the burden of factually supporting any *prima facie* conclusion of obviousness. In sustaining a rejection under 35 USC §103, the asserted combination must teach or suggest *each and every* feature of a claim. See, e.g. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974); *In re Wada and Murphy*, Appeal 2007-3733, citing *In re Ochiai*, 71 F.3d 1565, 1572 (Fed. Cir. 1995); *In re Wada and Murphy*, citing *CFMT, Inc. v. Yieldup Intern. Corp.*, 349 F.3d 1333, 1342 (Fed. Cir. 2003). Absent a teaching or suggestion, an obviousness rejection under 35 USC §103 cannot be maintained. In establishing a *prima facie* case, the Office must set forth “some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.” MPEP §2141 citing *KSR Int’l v. Teleflex Inc.*, 127 S.Ct. 1727 (2007). In determining the differences between the cited art and the claims, the question is not whether the differences themselves would have been obvious, *but whether the claimed invention as a whole* would have been obvious. See, e.g., *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530 (Fed. Cir. 1983). References relied upon to support a rejection under 35 USC §103 must provide enabling disclosure, i.e., they must place the claimed invention in the possession of the public. *In re Payne*, 606 F.2d 303 (C.C.P.A. 1979). Furthermore, according to MPEP §2141.02, the prior art must be considered in its entirety, including disclosures that teach away from an applicant’s claims. As the Examiner is well aware, “impermissible hindsight must be avoided and the legal conclusion must be reached on the basis of the facts gleaned from the prior art.” MPEP §2142. If the Examiner does not prove a *prima facie* case of unpatentability, then without more, the Applicant is entitled to the grant of the patent. See, e.g., *In re Oetiker*, 977 F.2d 1443.

The USPTO has recently provided further guidance on the issue of obviousness in its issuance of the *USPTO Examination Guidelines Update: Developments in the Obviousness Inquiry After KSR v. Teleflex*, Federal Register, Vol. 75, No. 169, Wed. Sept. 1, 2010.

Applicants respectfully contend that, applying these guidelines, a conclusion of nonobviousness of the claims now pending is clearly established.

With respect to forming a proper rejection based on a combination of elements, the recently issued Guidelines clarify that

... merely pointing to the presence of all claim elements in the prior art is not a complete statement of a rejection for obviousness. In accordance with MPEP §2143 A(3), a proper rejection based on the rationale that the claimed invention is a combination of prior art elements also includes a finding that results flowing from the combination would have been predictable to a person of ordinary skill in the art. MPEP §2143 A(3). If results would not have been predictable, Office personnel should not enter an obviousness rejection using the combination of prior art elements rationale, and should withdraw such a rejection if it has been made.

USPTO Examination Guidelines Update, emphasis supplied.

The guidelines also make clear that “a hallmark of a proper obviousness rejection based on combining known prior art elements is that one of ordinary skill in the art would reasonably have expected the elements to maintain their respective properties or functions after they have been combined.” *USPTO Examination Guidelines Update*, emphasis supplied. Finally, Applicants note that the Guidelines clarify that “the ‘predictable result’ discussed in *KSR* refers not only to the expectation that prior art elements are capable of being physically combined, but also that the combination would have worked for its intended purpose.” *Id.* The Guidelines state that “it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does.” *USPTO Examination Guidelines Update*, citing *KSR*, emphasis supplied.

Reviewing the clarified standard as recently clarified and reiterated by the USPTO, Applicants contend that a finding of nonobviousness is required in view of the documents cited by the Office, and that the rejection under 35 USC §103 must be withdrawn. In particular, independent claim 71 recites

A method of manufacturing a rapid dissolving tablet suitable for buccal delivery of an active agent containing one or more active medicaments, comprising the steps of

(1) supplying a biologically acceptable carrier liquid through a first supply tube to an outlet of said first supply tube, said biologically acceptable carrier liquid comprising a solution of a biologically acceptable polymer;

(a) wherein said biologically acceptable polymer is selected from the group consisting of gelatin, polyvinyl pyrrolidone, vinylpyrrolidone/vinylacetate copolymer, vinylpyrrolidone/vinylimidazole copolymer, and polyvinyl alcohol in a mixture of water and ethanol; and

(b) wherein said water and ethanol are present in said carrier liquid at a ratio of from about 1:0.8 to about 1:1.5;

- (2) establishing an electric field between the outlet of said first supply tube and a support surface that is spaced from the outlet to cause liquid issuing from the outlet to form at least one fiber or fibrils of said carrier liquid;
- (3) causing said fibers or fibrils to deposit onto the support surface to form a fibrous porous web or mat;
- (4) supplying a biologically acceptable carrier liquid comprising an active medicament through a second supply tube to an outlet of said second supply tube;
- (5) applying a charge to said carrier liquid of Step 4 opposite the charge of said first electric field of Step 2 to form a layer of fibers or fibrils comprising said active ingredient on top of said fibrous porous web or mat from Step 3;
- (6) repeating Steps 1- 3 so as to deposit a layer of fibers or fibrils on the surface of the layer of fibers or fibrils of active ingredient from Step 5; and
- (7) forming a plurality of individual tablets from the layers produced from step 6; and

wherein the individual tablets are capable of rapid dissolution suitable for buccal delivery.

As stated above, to establish a *prima facie* case of obviousness, the Office must show some finding that results flowing from the combination would have been predictable to a person of ordinary skill in the art. Applicants respectfully contend that no such showing is made. Specifically, Applicants contend that the Coffee document generally teaches the manufacture of items that should not dissolve rapidly, such as webs and mats for the purpose of wound dressing, and “capsules” or “microcapsules”, which Applicants contend are not rapidly dissolving and cannot be considered analogous to the recited dosage forms. Further, the disclosed microcapsules are suspended in a liquid, and as such, cannot be rapidly dissolving. The Office asserts that Liu teaches specific deficiencies in the primary reference (Coffee) such as the manufacture of tablets that can comprise polyvinylpyrrolidone and rapidly disintegrating tablets, that Barabas teaches the production of ibuprofen complexes with the vinylpyrrolidone copolymer, and that Murray teaches a process for preparing fast-disintegrating dosage forms comprising a carrier and an active ingredient wherein the carrier is fish gelatin. Applicants contend, however, that there is no showing that the results from these combined references would have been predictable to a person of ordinary skill in the art, particularly in view of the “teachings away” cited below. If such results *would not have been predictable*, Office personnel should not enter an obviousness rejection using the combination of prior art elements rationale, and should withdraw such a rejection if it has been made. Applicants respectfully contend that such is the case at bar. Withdrawal of the rejection under 35 USC §103 for at least these reasons is respectfully requested.

The above notwithstanding, Applicants further contend that there is no proper showing by the Office of why one of ordinary skill in the art would have been prompted to combine the elements in the way the recited invention does. At best, assuming the disclosure of “capsules” or “microcapsules”, Applicants contend that there is no showing why one in the relevant field of manufacturing *rapidly dissolving dosage forms* would look to the electrohydrodynamic comminution methods disclosed by Coffee to arrive at the claimed invention. In fact, Applicants contend that the art as a whole *teaches away* from Applicants invention, and that further, modifying the primary reference would render the subject matter of the primary reference

unsuitable for its intended purpose. As such, the instant invention is nonobvious in view of these teachings. In support, Applicants contend that *at least* the following portions of the cited documents support a conclusion of non-obviousness in these respects:

- Coffee et al. teaches the manufacture of webs/mats for covering surfaces such as wounds (p.17-18); as previously stated, it would *not* be desirable for such coverings to be rapidly dissolvable, thus teaching away from the combination, and further, making such coverings rapidly dissolvable would render the wound coverings of Coffee unsuitable for their intended purpose.
- Coffee et al. teaches that the resulting material, when in the form of fibrils, may actually “stick to the surface, for example, skin or soft tissue...” (p. 23.) Applicants contend that a material that sticks to skin or soft tissue would not be desirable in the manufacture of rapidly dissolving tablets suitable for buccal delivery as presently claimed, also teaching away from Applicants’ invention.
- Coffee et al. discloses methods for the manufacture of microcapsules for inhalation (p.29) that may be suspended in a liquid (p.25). Accordingly, modifying the microcapsules of Coffee such that the microcapsules are rapidly disintegrating would render the subject matter of Coffee unsuitable for its intended purpose.
- Liu et al. teaches that “many tablet manufacturing processes use organic solvents, thereby leaving unwanted and undesirable organic solvent residues in the final tablet formulation” and “*it would further be advantageous if such tablets could be made ... without the use of organic solvents.*” Emphasis added. In contrast, independent claim 71 *requires* the presence of ethanol in forming the rapidly dissolving tablets using electrohydrodynamic comminution. Thus, Applicants contend this is an express teaching away from the combination asserted by the Office.
- The Examples of Murray (*See, e.g.,* Examples 1-4) suggest that water is the only suitable solvent for preparing the disclosed dosage forms, further suggesting—in view of Liu et al.’s teachings with regard to tablet processes—that the solvents of the claimed invention would be unsuitable.

Net, as set forth above, Coffee generally discloses methods and products that cannot and should not dissolve rapidly, such as wound coverings and microcapsules that are suspended in liquid. Applicants contend that modifying the subject matter of Coffee to arrive at the claimed invention renders Coffee unsuitable for its intended purpose, thus rebutting any *prima facie* case of obviousness. Applicants further note that this is not an attempt to attack the references individually, as suggested by the Office, but rather, is merely Applicants pointing out teachings in the references that properly support a conclusion of nonobviousness. Applicants further respectfully contend that those “teachings away” set forth in Applicants’ prior response were not accorded proper weight in the instant Office Action, and respectfully request careful consideration of these teachings as is required by the MPEP and applicable caselaw.

Accordingly, for at least the foregoing reasons, Applicants respectfully contend that a *prima facie* conclusion of obviousness cannot be properly supported and/or is rendered inapplicable. Withdrawal of the rejection of the claims under 35 USC §103 and reconsideration and allowance of the claims is respectfully requested.

Clarification of the Record

Applicants further wish to clarify the record with respect to the Office’s interpretation of Applicants’ remarks. Applicants did not state, or intend to state, in the prior response that “the Coffee application does contain a disclosure for ingestible capsules that may be formed by the EHD process, suitable for oral administration,” such that it is proper for the Examiner to interpret the disclosure of Coffee to read on the limitation of forming *tablets* as recited in the instant claims. To the extent the Office is referring to Applicants’ statement in the prior response that “... Coffee et al disclose methods for the manufacture of microcapsules for inhalation ... that may be suspended in a liquid” (Response dated February 1, 2010), this statement is in no way intended to be, or should be construed as, an admission of a disclosure of tablets suitable for oral administration, particularly tablets having the properties described by the instant claims. In fact, Applicants contend that “microcapsules” are distinct from both capsules and tablets for a variety of reasons, and would not be exchangeable terms to one of skill in the art. Should the Office require evidence in support of the difference in such terms, Applicants will provide such evidence to the Office. Further, the above-notwithstanding, the instant disclosure relates

specifically to tablets for rapid buccal dissolution, which are distinct from ingestible tablets. Accordingly, Applicants respectfully contend that any conclusion based on such alleged "admission" is improper.

Applicants further note that the Office has argued that "optimization of bisphosphonate concentration would have been obvious at the time of Applicant's invention" and that evidence of unexpected results would be necessary to demonstrate nonobviousness. (Office Action, page 6, first paragraph.) Applicants' claims do not recite bisphosphonate. Accordingly, absent clarification by the Office, Applicants assume that such rejection is in error, and as such, have not addressed this rejection herein. Should Applicants' understanding be in error, the Office is invited to contact the undersigned attorney to clarify the rejection on this basis.

CONCLUSION

While several distinctions have been noted over the art of record, Applicant notes that there may be other limitations recited in the present claims which are neither taught nor suggested by the art of record. Applicant expressly reserves all rights and arguments with respect to distinctions not explicitly noted herein. In addition, to the extent that the amendments constitute a narrowing of the claims, such narrowing of the claims should not be construed as an admission as to the merits of the prior rejections. Indeed, Applicant traverses the rejections and preserves all rights and arguments.

With regard to all claims not specifically mentioned, these are believed to be allowable not only in view of their dependency on their respective base claims and any intervening claims, but also for the totality of features recited therein. The absence of additional patentability arguments should not be construed as either a disclaimer of such arguments or that such arguments are not believed to be meritorious. To the extent that any particular statement or argument by the Office in the pending Office Action has not been explicitly addressed herein, the same should not be construed as an acquiescence or admission by the Applicant that such statements or arguments by the Office are accurate or proper.

Based on the foregoing, all pending claims are in a condition for allowance. Accordingly, Applicant respectfully requests reconsideration and an early notice of allowance. Should the

Examiner wish to discuss the amendments or arguments made herein, Applicant invites the Examiner to contact the undersigned at (513) 369-4811 or via e-mail at ntepe@fbtlaw.com.

Respectfully submitted,
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